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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|------------------|-------------|----------------------|---------------------|------------------|
| 10/076,071 | 02/13/2002 | David Bar-Or | 4172-3-2 | 8825 |
| 22442 | 7590 | 12/26/2007 | EXAMINER | |
| SHERIDAN ROSS PC | | | DESAI, ANAND U | |
| 1560 BROADWAY | | | | |
| SUITE 1200 | | | ART UNIT | PAPER NUMBER |
| DENVER, CO 80202 | | | 1656 | |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | |
|------------------------------|-----------------------|---------------|
| Office Action Summary | Application No. | Applicant(s) |
| | 10/076,071 | BAR-OR ET AL. |
| | Examiner | Art Unit |
| | Anand U. Desai, Ph.D. | 1656 |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 03 October 2007.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 531-542, 547, 548, 550-552, 555, 558, 560, 569-576 and 581 is/are pending in the application.
 - 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 531-542, 547, 548, 550-552, 555, 558, 560, 569-576, and 581 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

| | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____. |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____. | 6) <input type="checkbox"/> Other: _____. |

DETAILED ACTION

1. This office action is in response to Amendment filed on October 3, 2007. Claims 544, 545, 546, 553, 554, 559, 561-568, and 577-580 have been cancelled. New claim 581 has been added. Claims 531-542, 547, 548, 550-552, 555, 558, 560, 569-576, and 581 are currently pending and are under examination.

Withdrawal of Rejections

2. The rejection of claims 531-539, 560, and 569-576 under 35 U.S.C. 103(a) as being unpatentable over Harford and Sarkar (Acc. Chem. Res. 30: 123-130 (1997); previously cited) in view of Hu, G. (Journal of Cellular Biochemistry 69: 326-335 (1998)) is withdrawn based on the amendment to incorporate the limitation of claim 546 into claim 531.

Maintenance of Rejections

Claim Rejections - 35 USC § 112, Enablement

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 531-542, 547, 548, 550-552, 555, 558, 560, 569-576, and 581 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating an angiogenic disease or condition in an animal by inhibiting angiogenesis using metal-binding peptides as disclosed in the examples and the declaration filed April 20, 2006, does not reasonably provide enablement for a method of treating an angiogenic disease or condition with

a metal-binding peptide encompassed by the formula, P₁-P₂; P₁ is Xaa₁ Xaa₂ His or Xaa₁ Xaa₂ His Xaa₃, the P₁ portion of the peptide is linear, P₂ is any metal binding sequence that contains no more than 10 amino acid residues, and Xaa₁, Xaa₂, Xaa₃, and Xaa₄ are amino acids disclosed in claim 531. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The rejection was explained in the office action mailed September 30, 2005, and further discussed in the office action mailed July 25, 2006 and April 4, 2007.

Response to Remarks

5. The claims are drawn to a method of treating an angiogenic disease or condition in an animal comprising administering to the animal an amount of a metal-binding peptide which does not have a metal bound to it or a physiologically-acceptable salt of the peptide, the amount of the peptide or salt which is administered to the animal being effective to inhibit angiogenesis, the sequence of the peptide being P₁-P₂; P₁ is Xaa₁ Xaa₂ His or Xaa₁ Xaa₂ His Xaa₃, the P₁ portion of the peptide is linear, P₂ is any metal binding sequence that contains no more than 10 amino acid residues, and Xaa₁, Xaa₂, Xaa₃, and Xaa₄ are amino acids disclosed in the claims.

Applicant's arguments filed October 3, 2007 have been fully considered but they are not persuasive. The issue in this application is the breadth of the claims in light of the predictability of the art as determined by the number of working examples, the skill level artisan and the guidance presented in the instant specification and the prior art of record. This make and test position is inconsistent with the decisions of *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24

(CCPA 1970) where it stated that "...scope of claims must bear a reasonable correlation to scope of enablement provided by the specification to persons of ordinary skill in the art...".

Applicants Remarks dated September 7, 2005 state there was not sufficient predictability in the art of inhibiting angiogenesis using metal chelating agents at the time of the filing of the application (see also scope of enablement, section 3 of Office action mailed September 30, 2005). In reference to the presented claims, particularly P2 in claims 531 and 547 encompass a glycine amino acid residue at position Xaa₂, the prior enablement rejection describes the unpredictable nature of copper binding peptides with a glycine at position 2. The Lane, T et al. reference describes a peptide sequence, L-Lys-L-Gly-L-His-L-Lys, which stimulates angiogenesis (see scope of enablement, section 3 of Office action mailed September 30, 2005). Accordingly, there is unpredictability for metal-binding peptides ability to inhibit angiogenesis.

The HUVEC proliferation assay describes peptides, Tyr-Lys-His, Ser-Ser-His, D-Phe-Gly-His, and Asp-Ala-His-Arg-Arg-Arg-Arg-Arg-Arg that do not inhibit proliferation of endothelial cells, and do not inhibit angiogenesis.

Therefore, there is unpredictability for metal-binding peptides ability to inhibit angiogenesis. There is no way to predict whether all of the metal-binding peptides encompassed by the formulas in the claims will treat an angiogenic disease or condition by inhibiting angiogenesis. There is insufficient guidance and a large quantity of experimentation to make and use the peptides of the invention within the full scope of the claims.

Without sufficient guidance, determination of having the desired biological characteristics is unpredictable, and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. See *In re Wands*, 858 F.2d at 737, 8

USPQ2d at 1404 (Fed. Cir. 1988). Therefore, absent direction/guidance regarding whether the peptide can tolerate the modifications contemplated one of skill in the art would not be able to practice the claimed invention commensurate in scope with the claims.

Conclusion

6. No claims are allowed.
7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anand U. Desai, Ph.D. whose telephone number is (571) 272-0947. The examiner can normally be reached on Monday - Friday 9:00 a.m. - 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Kathleen Kerr Bragdon can be reached on (517) 272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

December 20, 2007

AD
/Anand Desai/
Patent Examiner
Art Unit 1656

/Robert B. Mondesi/
Primary Examiner
Art Unit 1652